Quantitative Review of Vaccine Policy: Integrating Science, Economics for Public Health

ADVAC Veyrier du Lac
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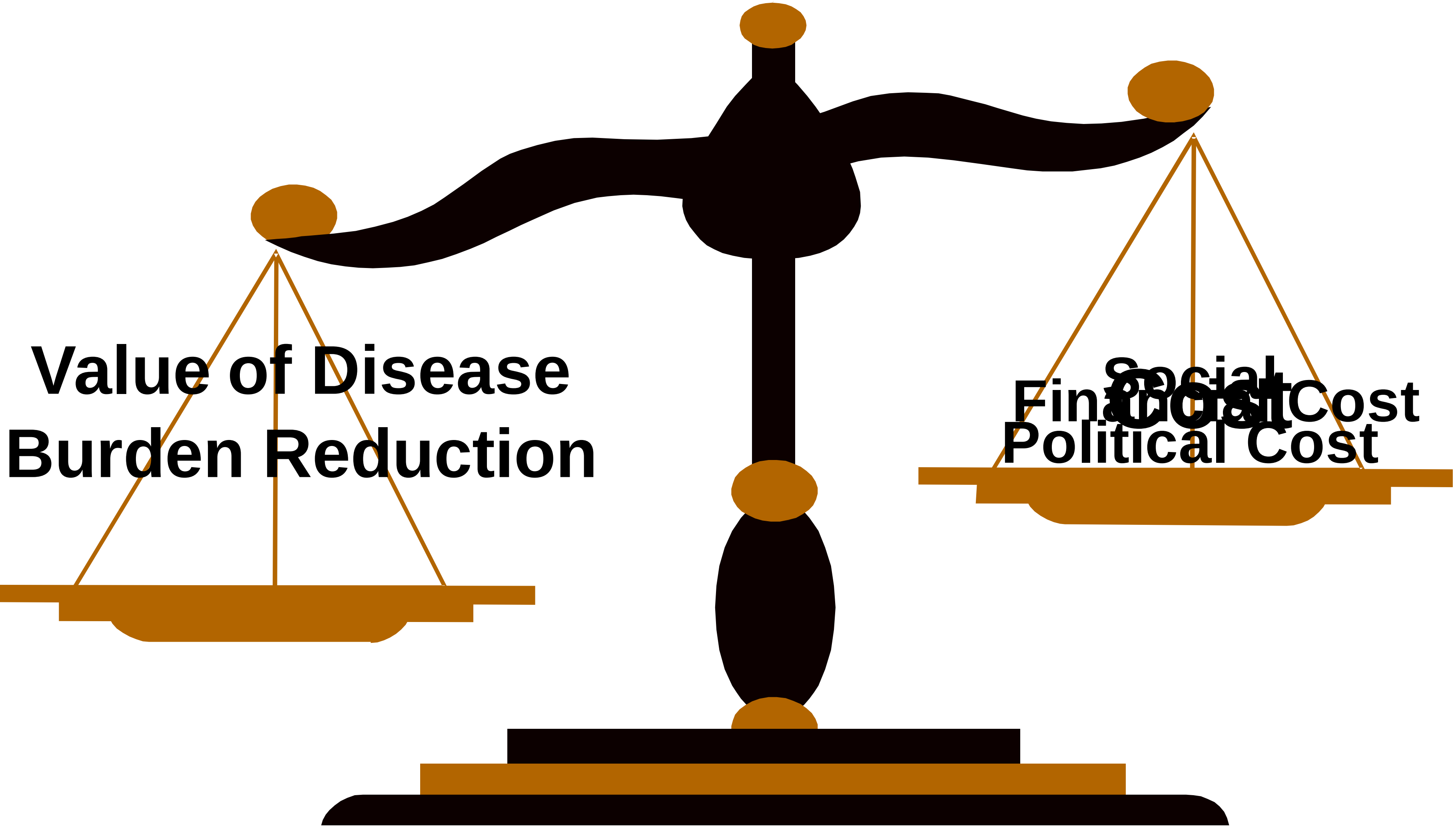
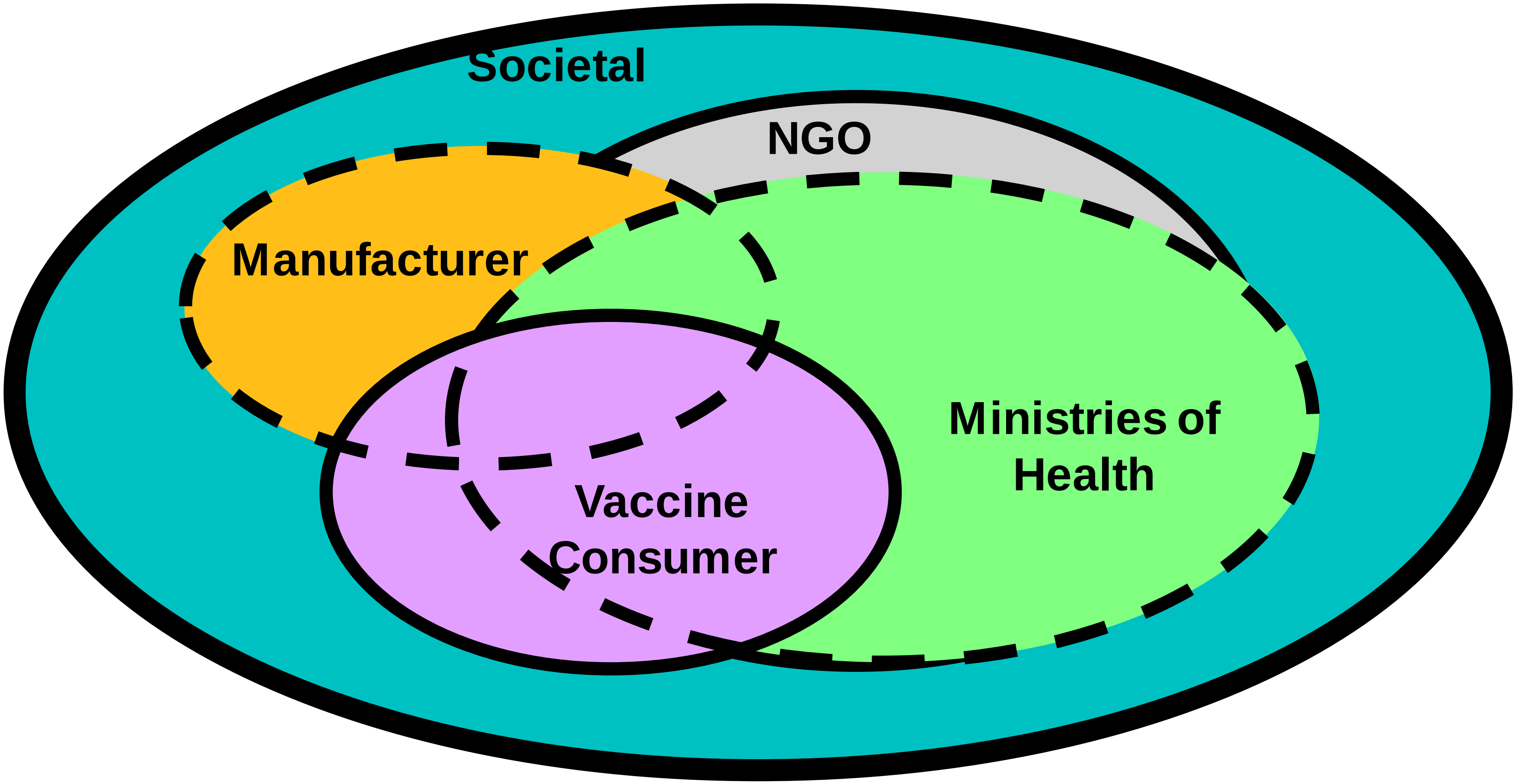
Objectives

- **Integration of epidemiology and economic inputs and outputs**
  - **Justification for investments for prevention and insurance policy**
- **Assessment of <u>value of health outcomes and</u> biological/ecological change**
  - **individual incentives**
  - **Justify public programs on population level**
- **Present options of strategies/health outcomes at various costs to systematically evaluate choices**
- **Evaluate uncertainty; value of specific research**
- **It's not just cost-effectiveness!**
  - **Limited resources, incentives, perception of values, business decisions, strategies**

Investing in Prevention: Vaccine Policy Assessments



Whose perspective?



Different accounting of costs and benefits

Simpler Times for Vaccine "Advocacy"

More Complex Today

- **Does incidence of SP specific serotypes, rotavirus, meningitis B or HPV justify vaccine intervention?**
  - **At what cost?**
  - **Relevant health outcomes (serotype replacement?)**
- **What is minimal level of effectiveness to justify vaccine use?**
  - **Sub-optimal performance--rotavirus, malaria**
  - **Influenza control**
- **What is value of "eradication", "elimination" vs expanded "control"**
  - **Poliomyelitis? Measles? Rubella – Real costs to <u>sustain eradication</u>**
- **Decision analysis for R&D investments to develop specific vaccines trade-off characteristics/attributes (performance, cost, ease of use)**
- **Economic evaluation not necessarily to provide answers but can identify critical inputs (research) for policy formulation**

Systems Approach to Prevention Effectiveness

No. Cases Prevented* = f*(Disease Burden, Efficacy, Coverage)

Surveillance
Literature

Changing incidence with control

technical

RCT
Post Licensure

political

economic

Coverage factors

technical = *f* ***(operational factors, program feasibility, human resources)***

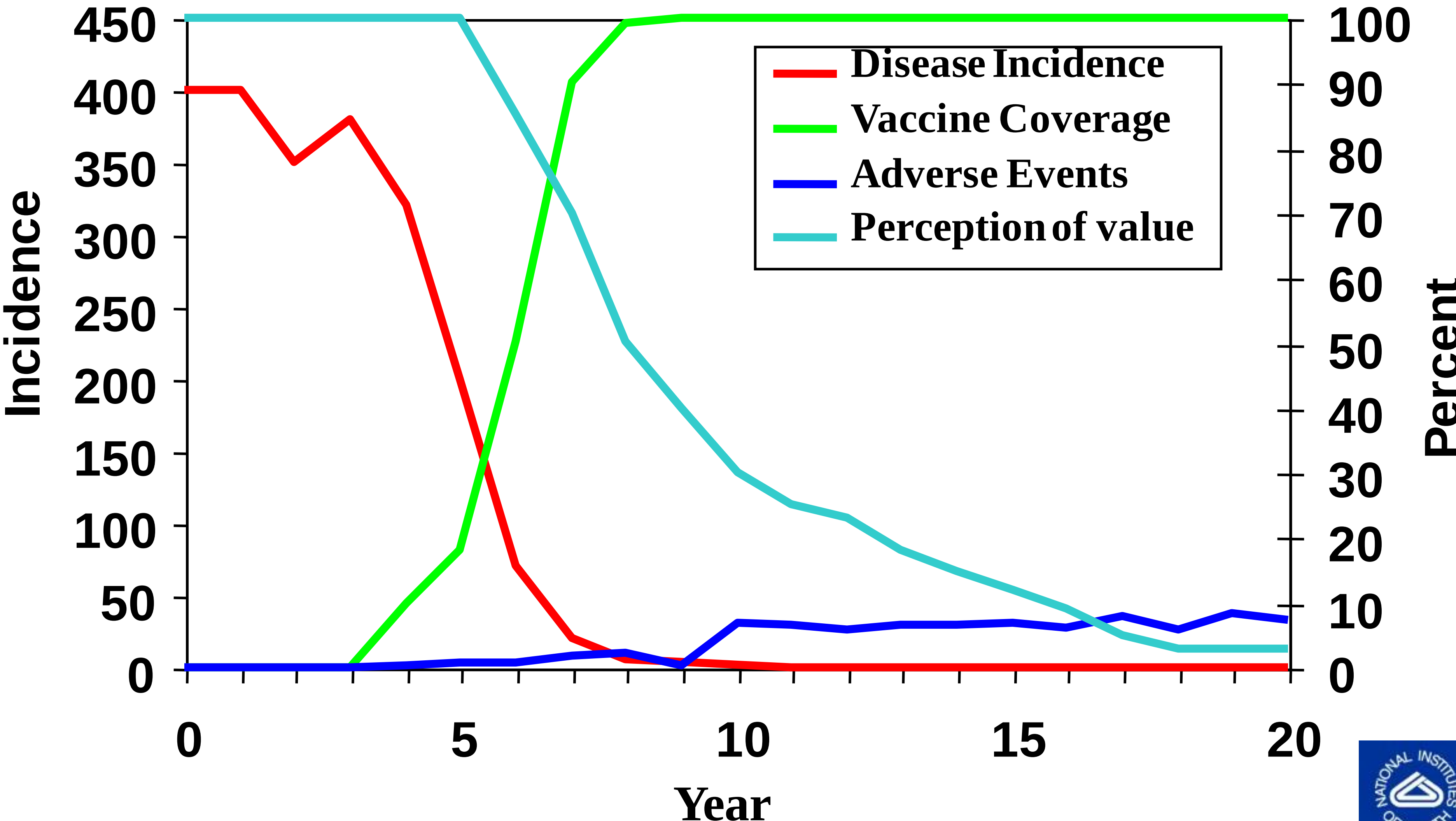
political = *f* ***(perception of disease burden, community)***

community acceptance = *f* ***(trust, education, coercion, mandate)***

economic = *f* ***(financial commitment, opportunity cost, Willingness to pay)***

All change with respect to time

Changing value perceptions over time (dynamic systems)



Data Matrix

Resolution

Spatial – global/national/administrative

Geographically defined units

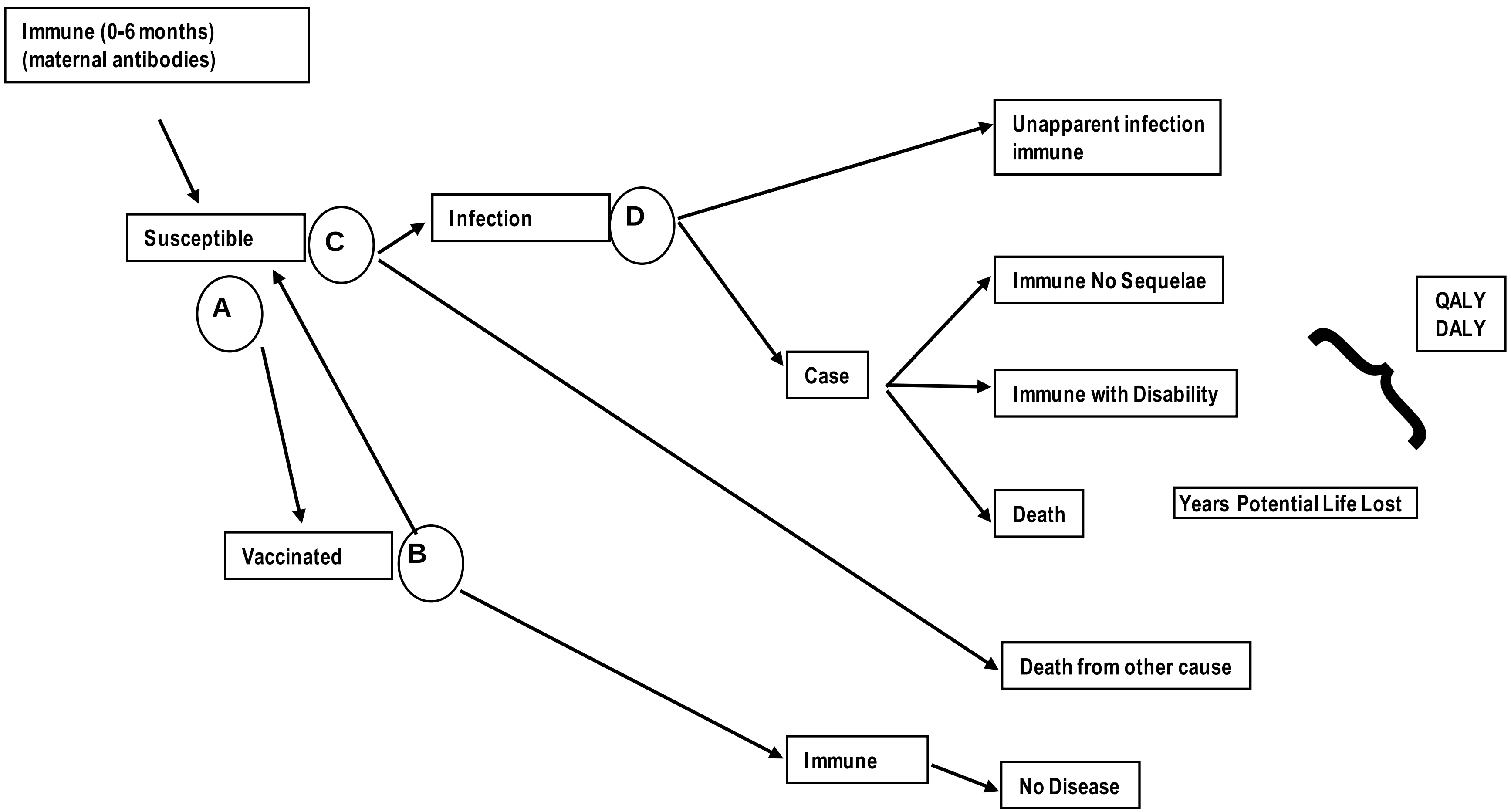
Temporal- decades/annual/seasonal/etc.

Data Types (determinants of disease and control)

Biology	Demographics	Environmental	Socio-behavioral	Logistical
Genetics	Age structure	Water access	Political	Human resources
Immunology	Population density	Sanitation	Community	Infrastructure
Ecology			Economic	Access

Basic Model Schematic

S I R Models



Transmission rates; incubation periods

What are Relevant Outcomes to Value

Outcome Metric	
Cases	Cases that occur or are prevented by an intervention. May be stratified by severity/sequelae
Deaths	Easily quantified but defies economic valuation. CEA often
Years of Potential Life Lost	Refines the death metric to also account for life expectancies and age of disease acquisition
Quality-adjusted life-years or Disability-adjusted life-years or other	Further refines by incorporating morbidity states and time with condition—useful for chronic disease outcomes
Outbreaks	Disruption of societal functions

Vaccine Intervention Accounting

- **Fixed administration**
  - Training
  - Personnel
  - Equipment
- **Recurrent**
  - Operating costs
  - Vaccine and wastage
  - Syringe and needle
- **Adverse events (Real or perceived)**

Who pays, who benefits?

Need to look at marginal cost to existing infrastructure

Disease Costs

- Microeconomic
  - Direct
    - Pharmaceuticals, diagnostic, provider, etc
    - Chronic disability (poliomyelitis, hepatitis, etc.)
  - Indirect
    - Lost wages (patient and care-givers)
  - Intangible
    - Social
    - Death
- Macro-economic
  - Example: tourism, agriculture
- Discounting (adjustment for time)

Quantify the Value of Prevention

- **Cost analysis** $(C_i - C_0)$
- **Cost Effectiveness** $(C_i - C_0)/\Delta$Health Outcome
- **Cost-Utility** $(C_i - C_0)/\Delta$Common Outcome
- **Cost-Benefit** (C - B or B:C ratio)
- **Decision Analysis** What if??
  - Alternative strategies/controls
- **Sensitivity Analysis** How robust?
  - Highlight research agenda

Example 1
Vaccine Introduction
Endemic Disease

Impact of *Haemophilus Influenzae* (HiB) Vaccine

Hib Data and Output
Bolivia (Prevaccine era 1997)

Demographics

Epidemiologic Assumptions

per cap GDP	births	<5 mortality	Coverage	Meningitis	Pneumonia
$760	257000	91	88%	30	150

(per 100,000 children <5)

Economic Assumptions (unit costs)

vaccine	admin	outpatient	hosp. Day
$2.30	$0.55	$11	$45

Output: Estimated disease burden

Meningitis	Pneumonia	Hospital Days	Hib Deaths
378	1892	9935	550

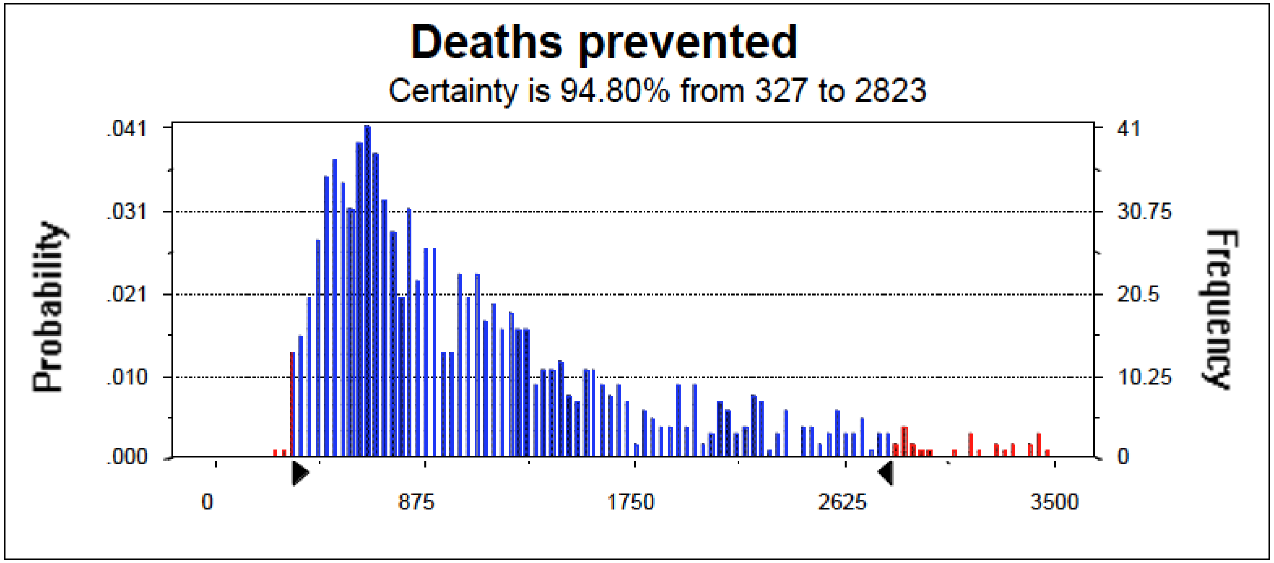
Disease Prevented

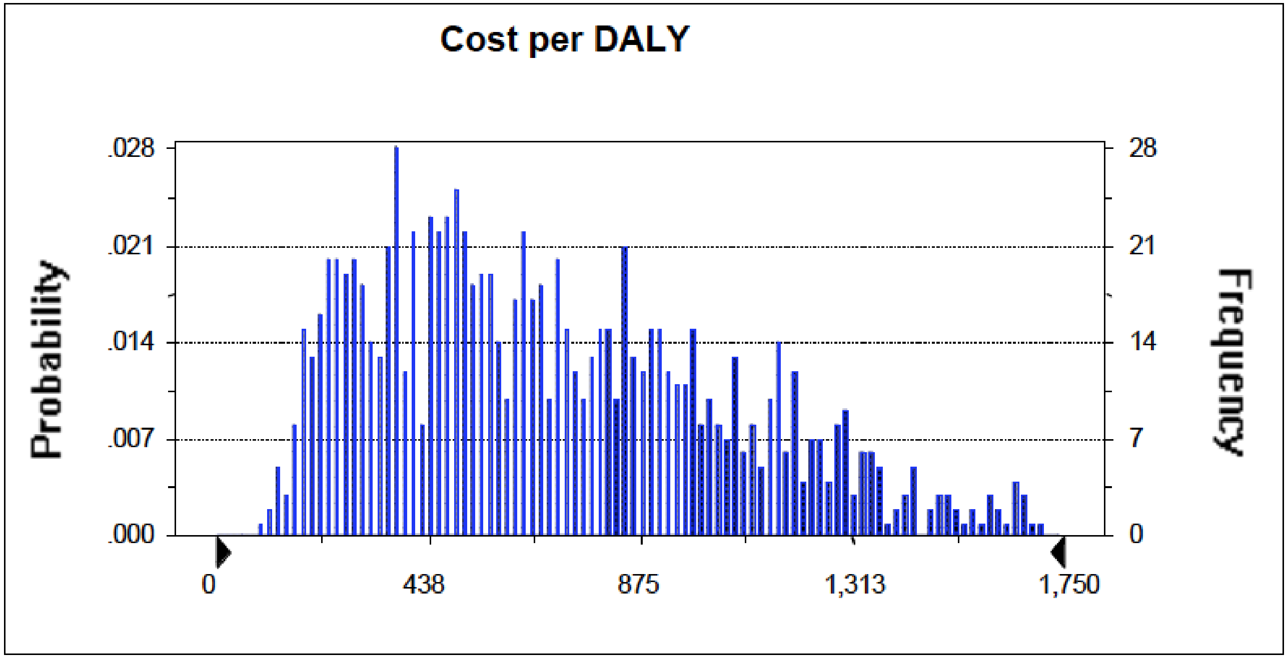
Meningitis	Pneumonia	Deaths	Life Years
316	1582	460	28 K

Economic Assessment

Vaccine	Admin	Total	Treatment savings	Cost per Year Life	% of per capita GDP
$1.6 M	$0.3 M	$1.9 M	$.4M	$55	7.2%

Simulation Results





1,000 Trials

Probability of value for each parameter given uncertainty of multiple variables

Example 2

Decision Analysis

Measles control strategies (1, 2 doses, campaigns?)

Immunity

Maternal antibody / **Vaccine efficacy**

Age (month)	Maternal antibody	Vaccine efficacy
0-5	100%	0%
6 to 8	30%	65%
) to 11	10%	85%
12+		95%

munity assumed at 1980: 93%

Apply default and non-country specific values

Force of Infection

depends on:

-Remote: No
-Income: Low
being above 93.3% between the age of 12-15 m to 20+ y

Case Fatality ratio

Country specific CFR: 4.000%

Age (year)	CFR multiplier	CFR
<1	2	8.000%
1-4	1	4.000%
5-9	0.5	2.000%
9>	0	0.000%

Vaccination

Use historic data: Yes

Complex

First Routine Doses

First year	
Periodicity (years)	
Age	
Coverage	
Cost/Unit	$0.99

Second Routine Doses

First year	
Periodicity (years)	
Age	
Coverage	
Cost/Unit	$1.20
Independence	50%

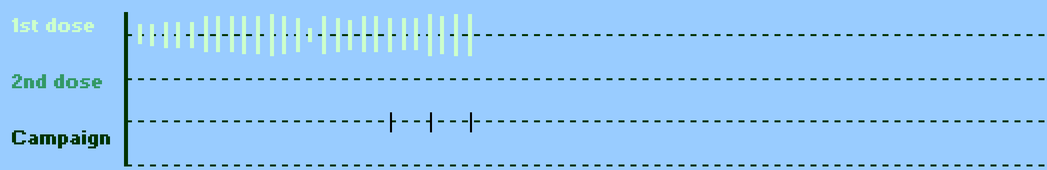
Vaccination campaign

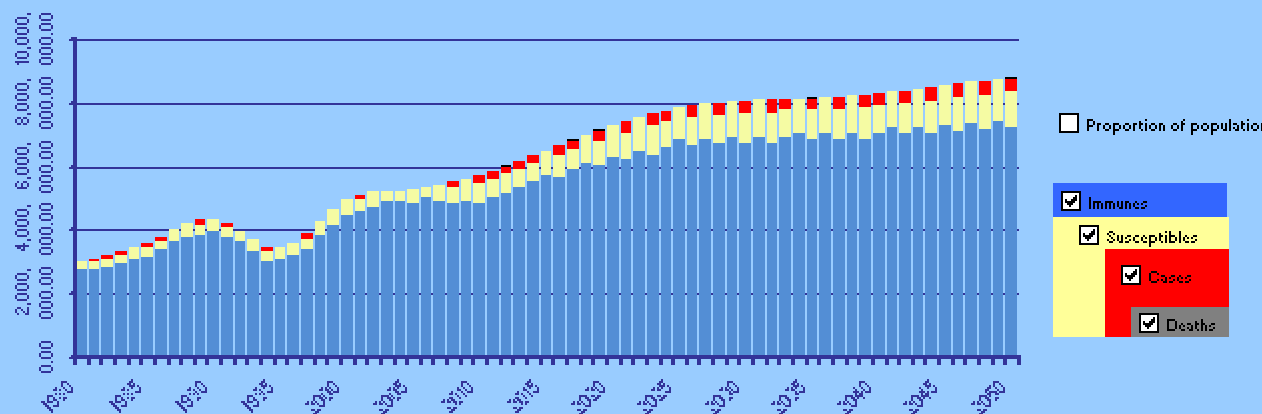
First year	
Periodicity (years)	
From age	
to age	
Coverage	
Cost/Unit	$0.77

Run Model

Compare with previous

Results





1980 — 2050

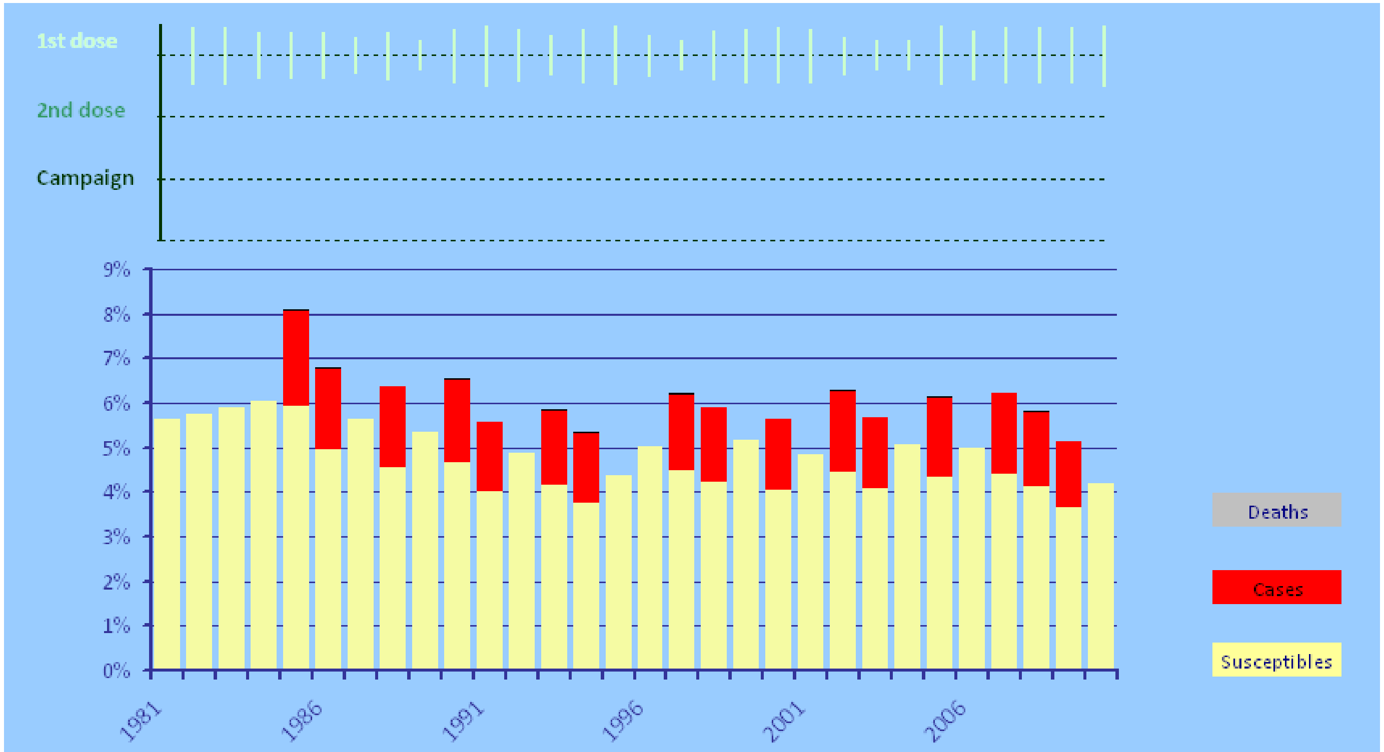
	Cases	Deaths
☑ 0 - 12 m	628,598	50,288
☑ 1 - 4 y	6,308,405	252,336
☑ 5 - 9 y	2,507,831	50,157
☑ 10 - 14 y	478,739	0
☑ 15 - 19 y	178,400	0
☐ 20+ y		
	10,101,973	352,781

Costs Vaccination

1st	$5,207,232
2nd	$0
Campaign	$2,685,128
Total	$7,892,360

Full Scre
Close Full

Analyses for Chhattisgarh (India) using historic vaccination data



Total results for the period 1981-2010 (last available historic record at 2007)

	Cases	Deaths
0-12 months	29,818	716
1-4 years	456,010	5,472
5-9 years	1,090,491	6,543
10-14 years	281,015	0
15-19 years	118,928	0
	1,976,263	12,731

	Costs Vaccination
1st	$2,387,134
2nd	$0
Campaign	$0
Total	$2,387,134

Various outcomes of immunology profiles and costs for different strategies

What is optimal??

Example 3
Policy Priorities

Evaluations to Prioritize Vaccine Options

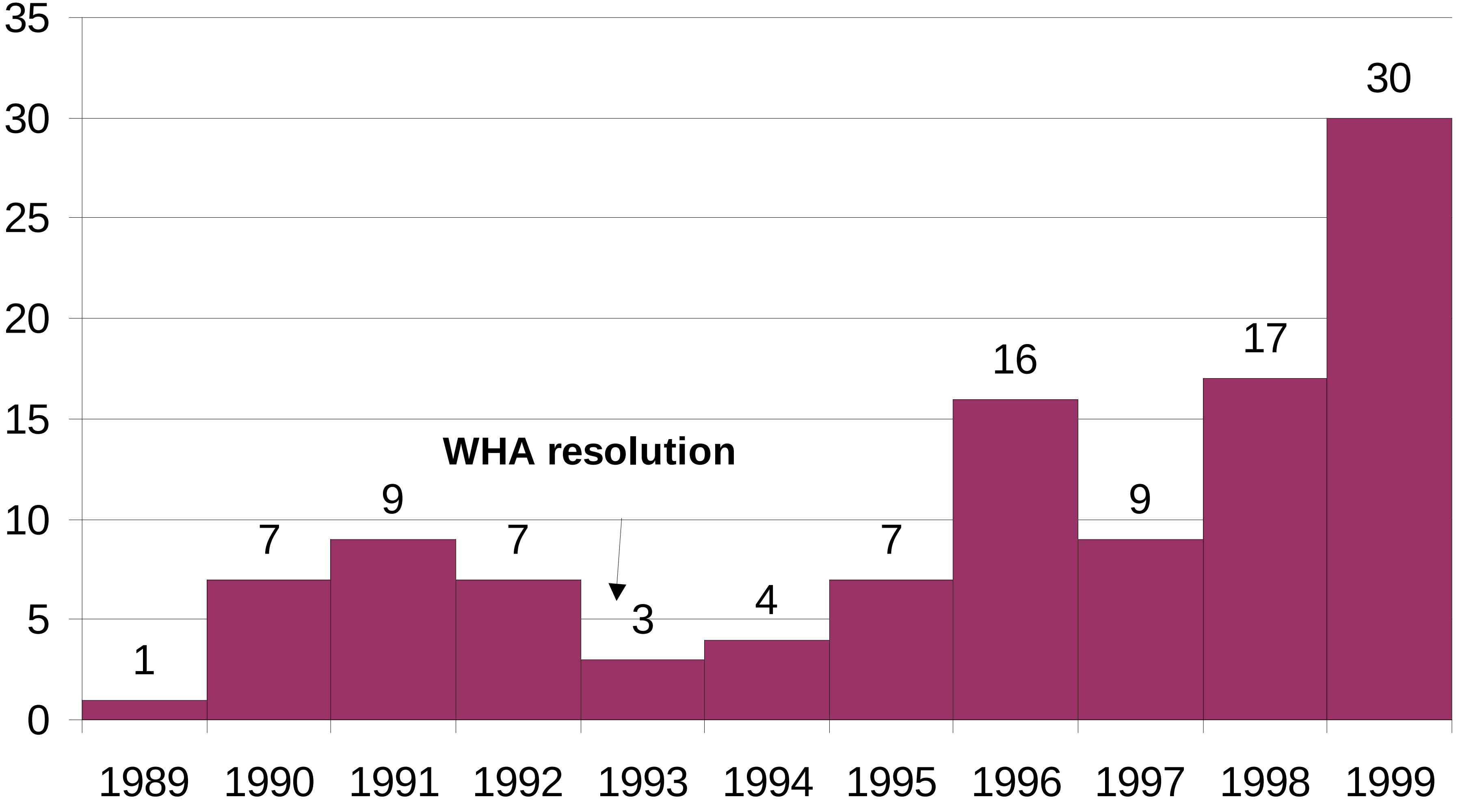
	Extending coverage			Introduction of new antigens, combo, boosters			
	Measles	Hep B	IPV	HPV	Men	DTPac	SP
Disease Burden							
Vaccine Program Costs							
Prevented Disease							
Treatment Savings							
Cost Effectiveness							

Although many vaccines have been considered cost-effective, why has there been a delay in their adoption into routine vaccination schedules in many countries?

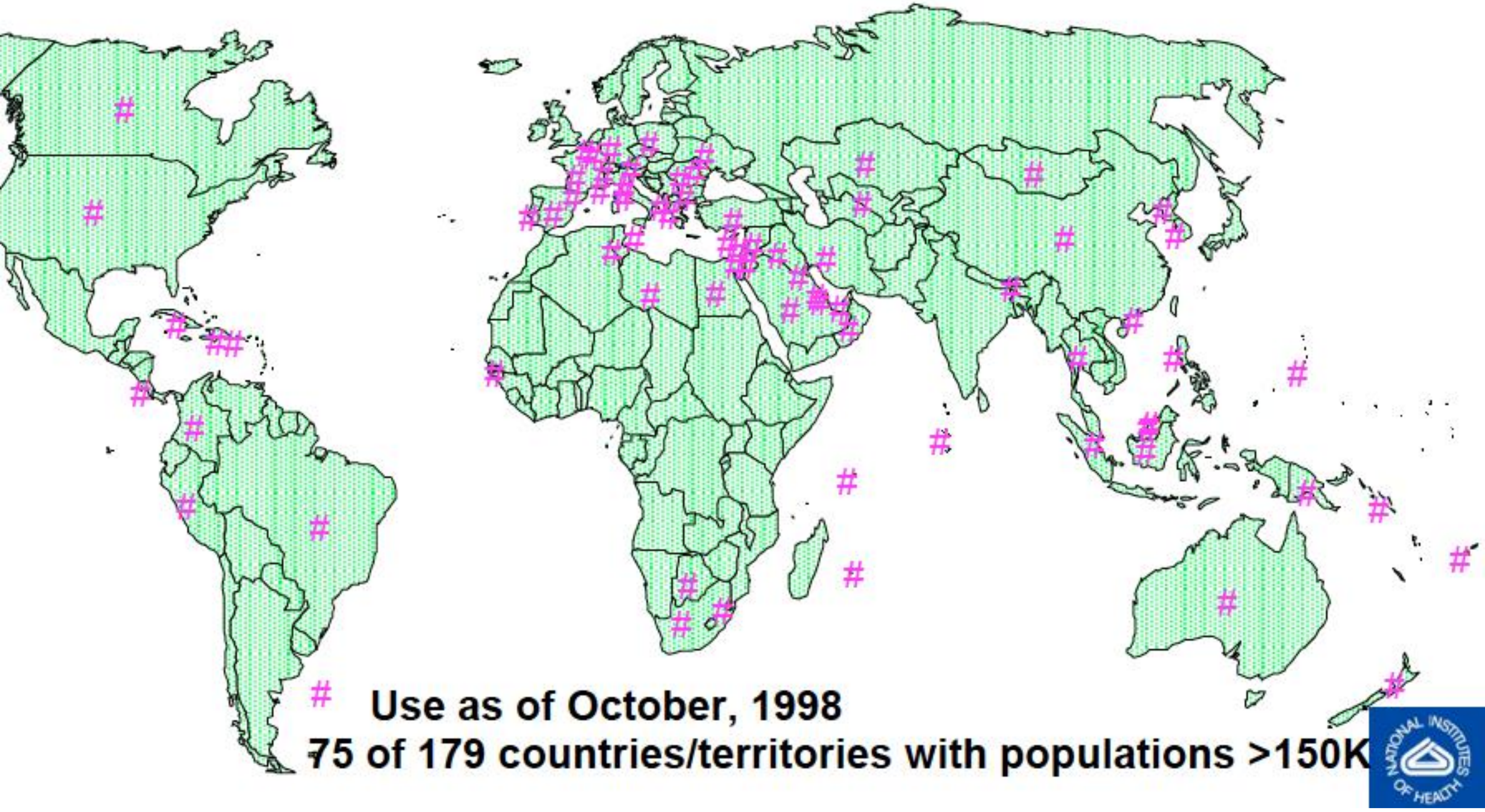
Example 4
Demand/Supply Prediction

Estimating the probability of national vaccine uptake (Hepatitis B, Hib)

Number of Countries Adopting Hepatitis B Vaccine into National Immunization Programs



Countries using hepatitis B vaccine in routine vaccination schedule



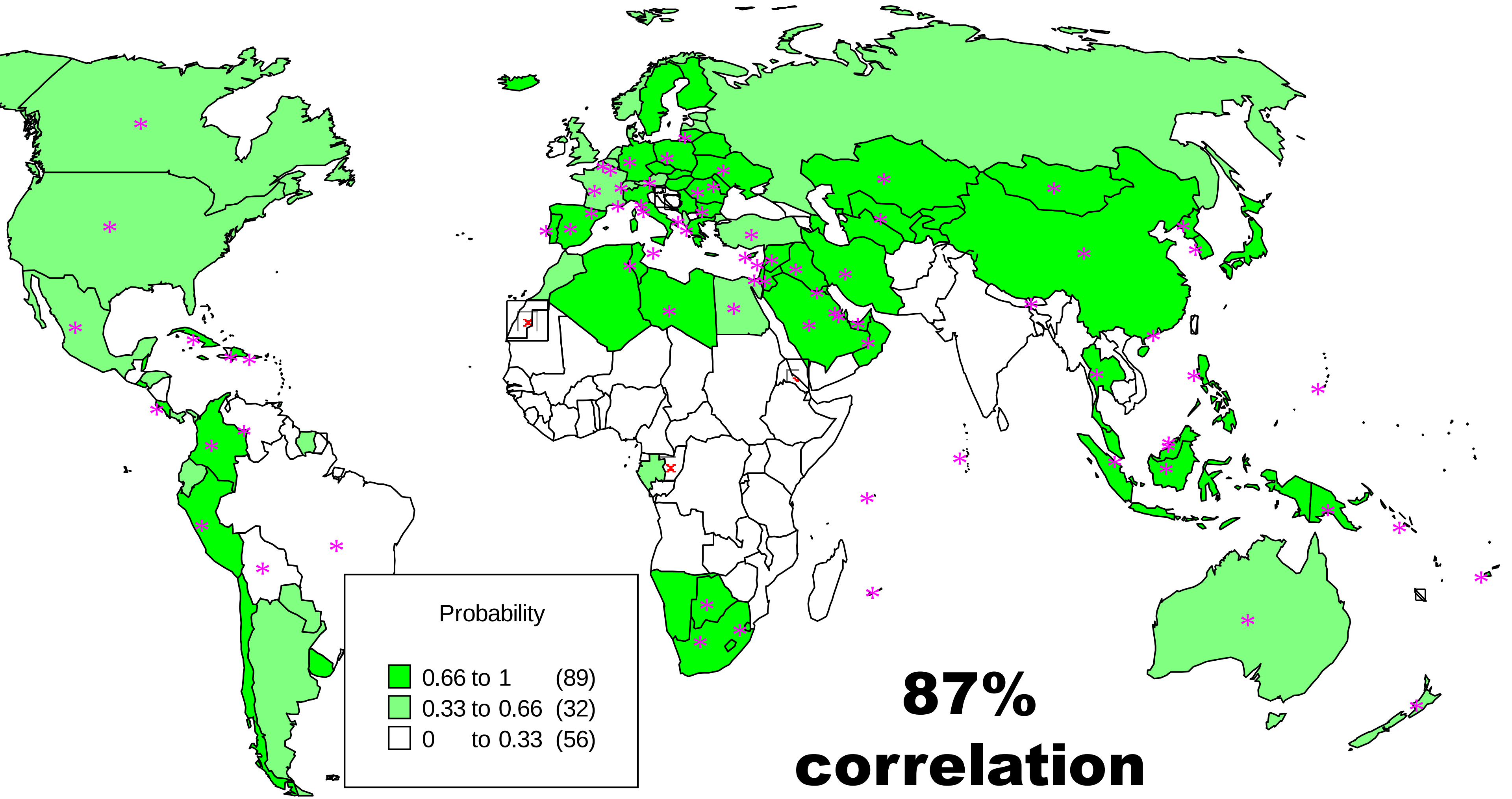
Factors associated with HB vaccine uptake into national schedules

Variable	Odds Ratio	95% Confidence intervals	
Treatment Cost	5.0	2.3	11.0
Years Life Lost (per capita)	6.9	2.9	16.1
Coverage	55.1	10.4	292.6
Per-capita GDP/ Vaccine cost	39.7	6.5	241.2

Highest quartile relative to lowest

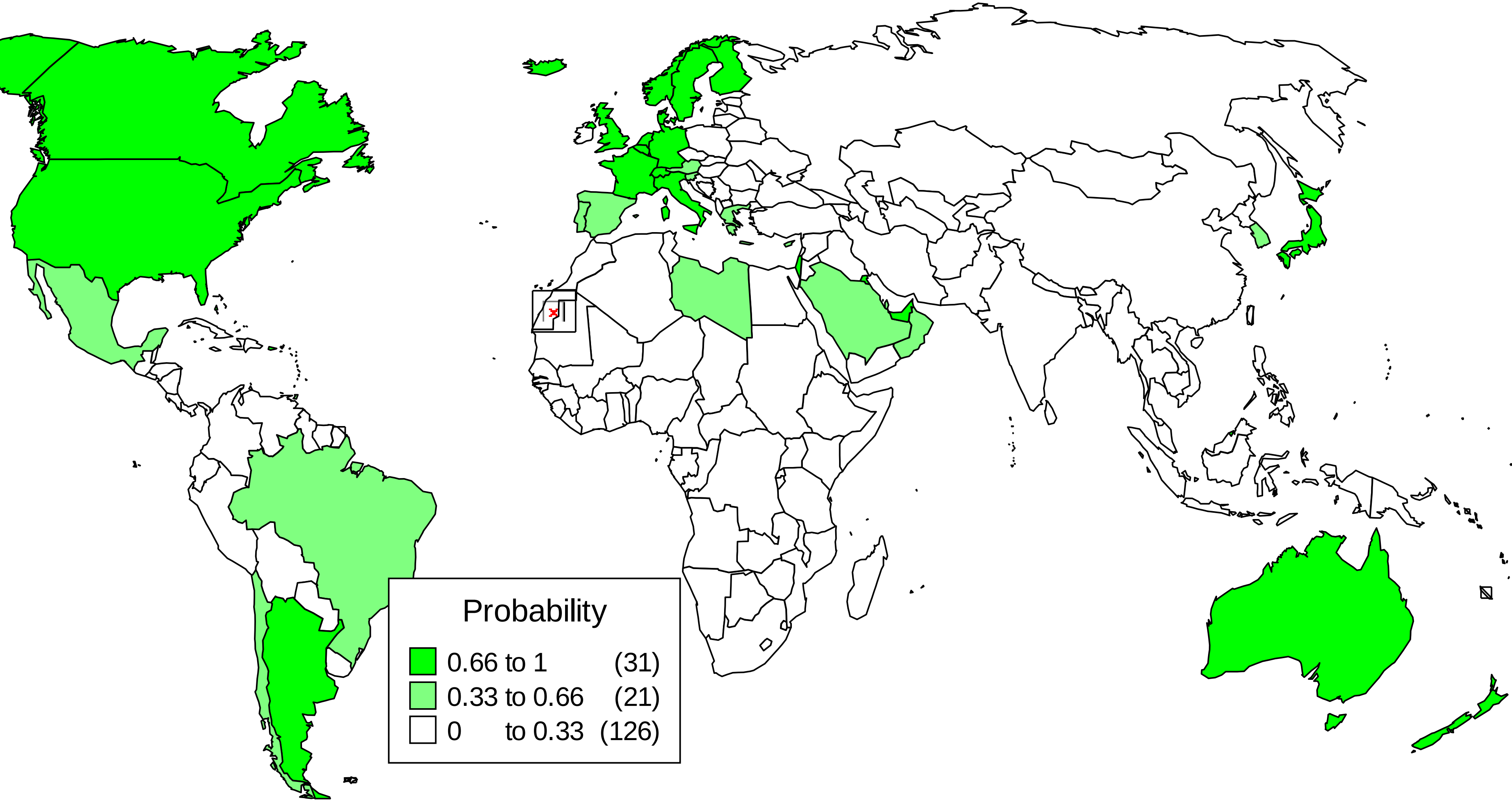
Miller MA, Flanders WD. A model to estimate the probability of hepatitis B- and Haemophilus influenzae type b-vaccine uptake into national vaccination programs. Vaccine. 2000

Estimated probability of hepatitis B vaccine uptake into national schedules

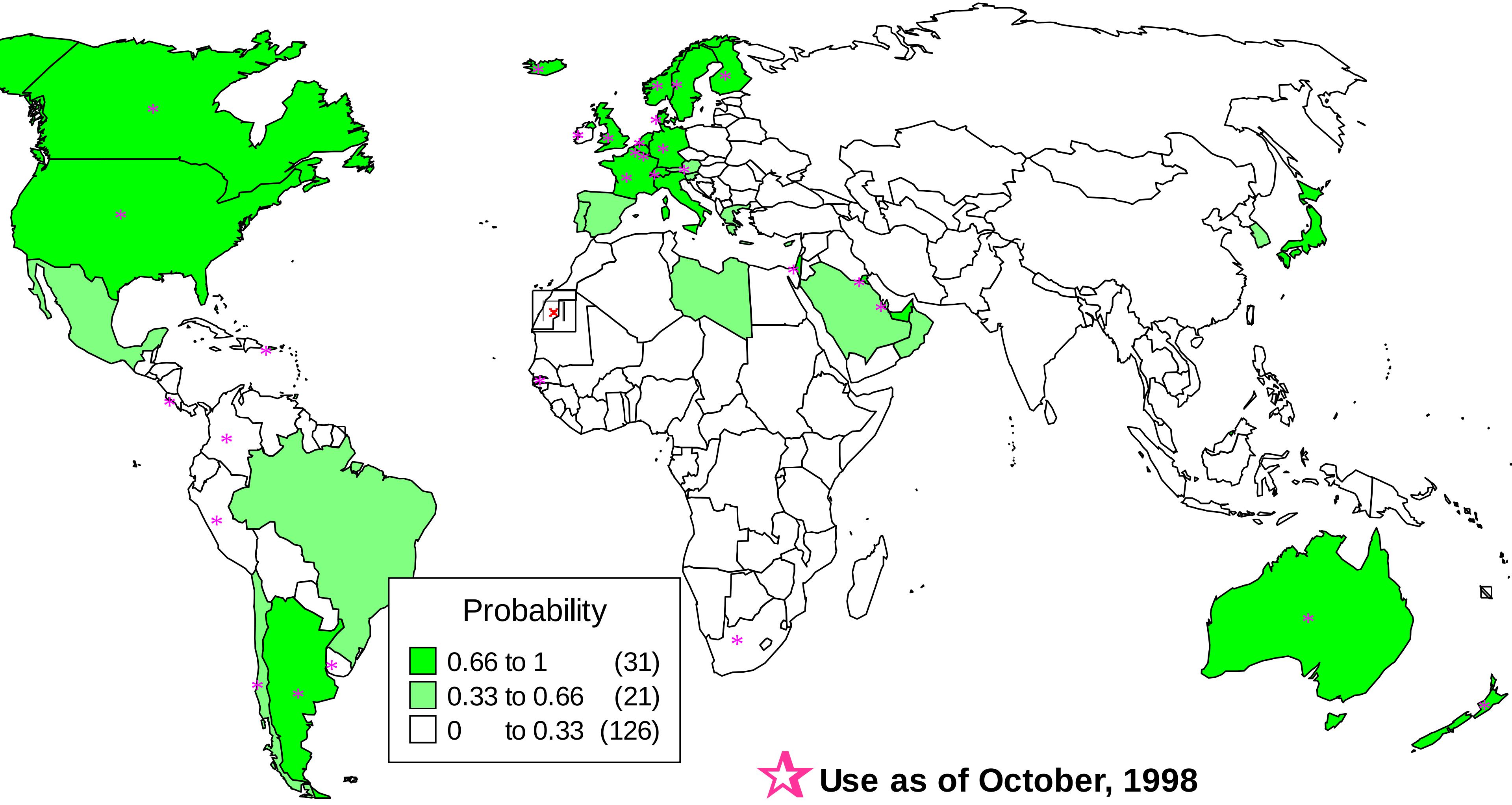


87% correlation

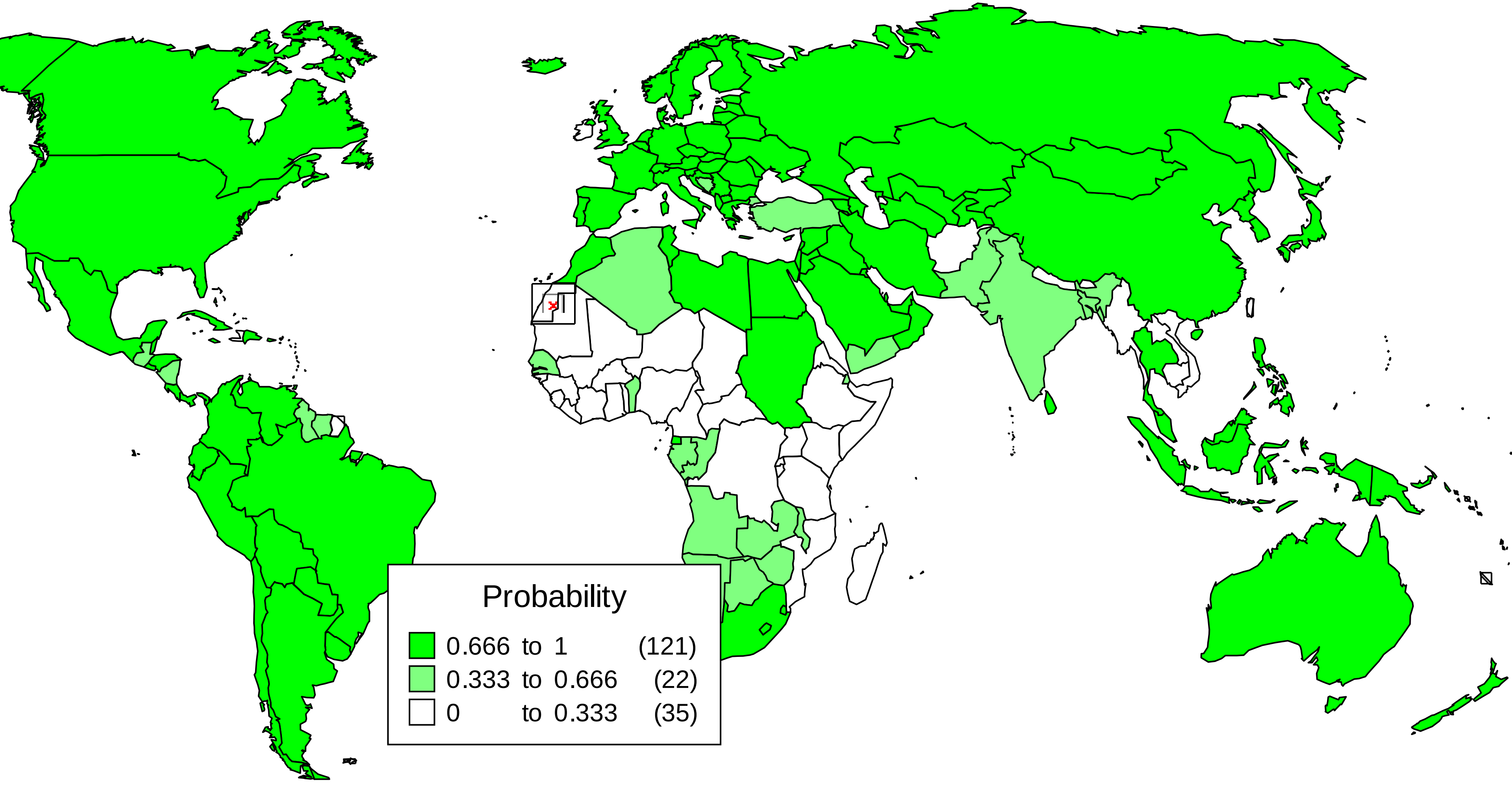
Estimated probability of Hib adoption



Estimated probability of Hib adoption and current actual use



Estimated probability of Hib adoption at 10% current cost



Factors to influence (short term)

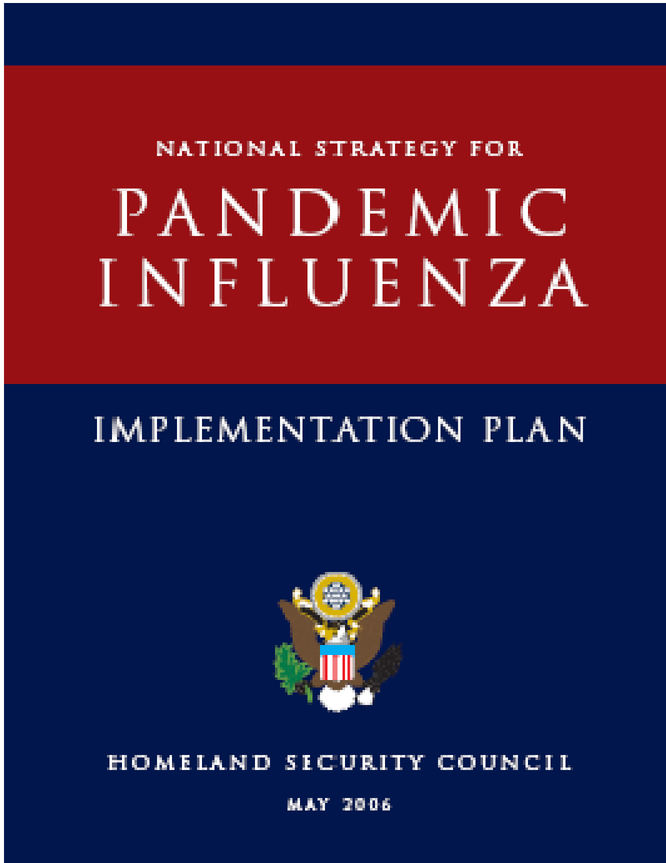
Factor	Audience
Coverage	Vaccine program, MOH, MOF, Communities, Management, Operational Research
Vaccine cost to public sector	Manufacturers Partner agencies
Perception of Disease Burden	MOH, MOF, Academia

Example 5
Influenza Pandemic

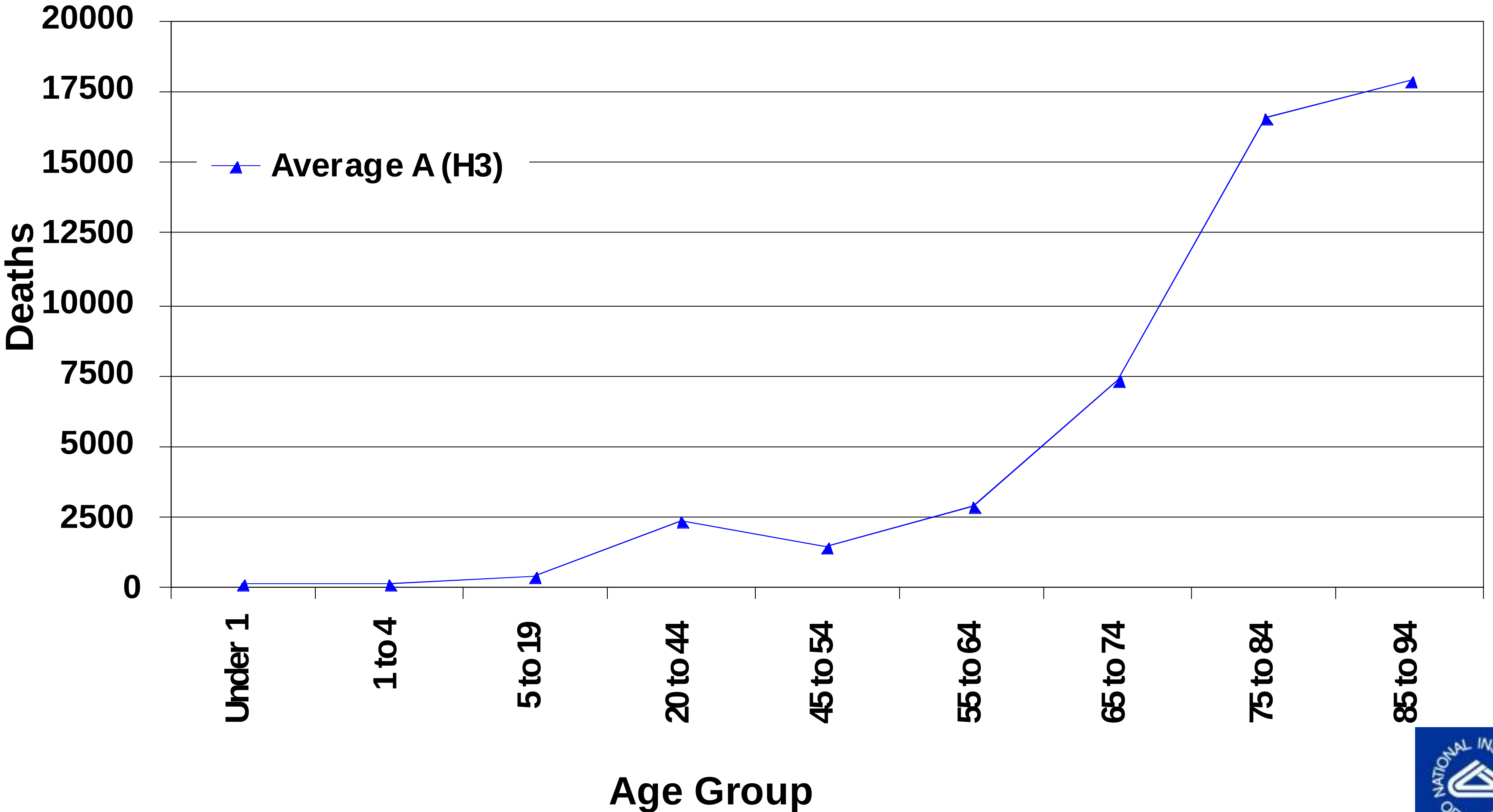
Planning of Potential Strategies

Objectives

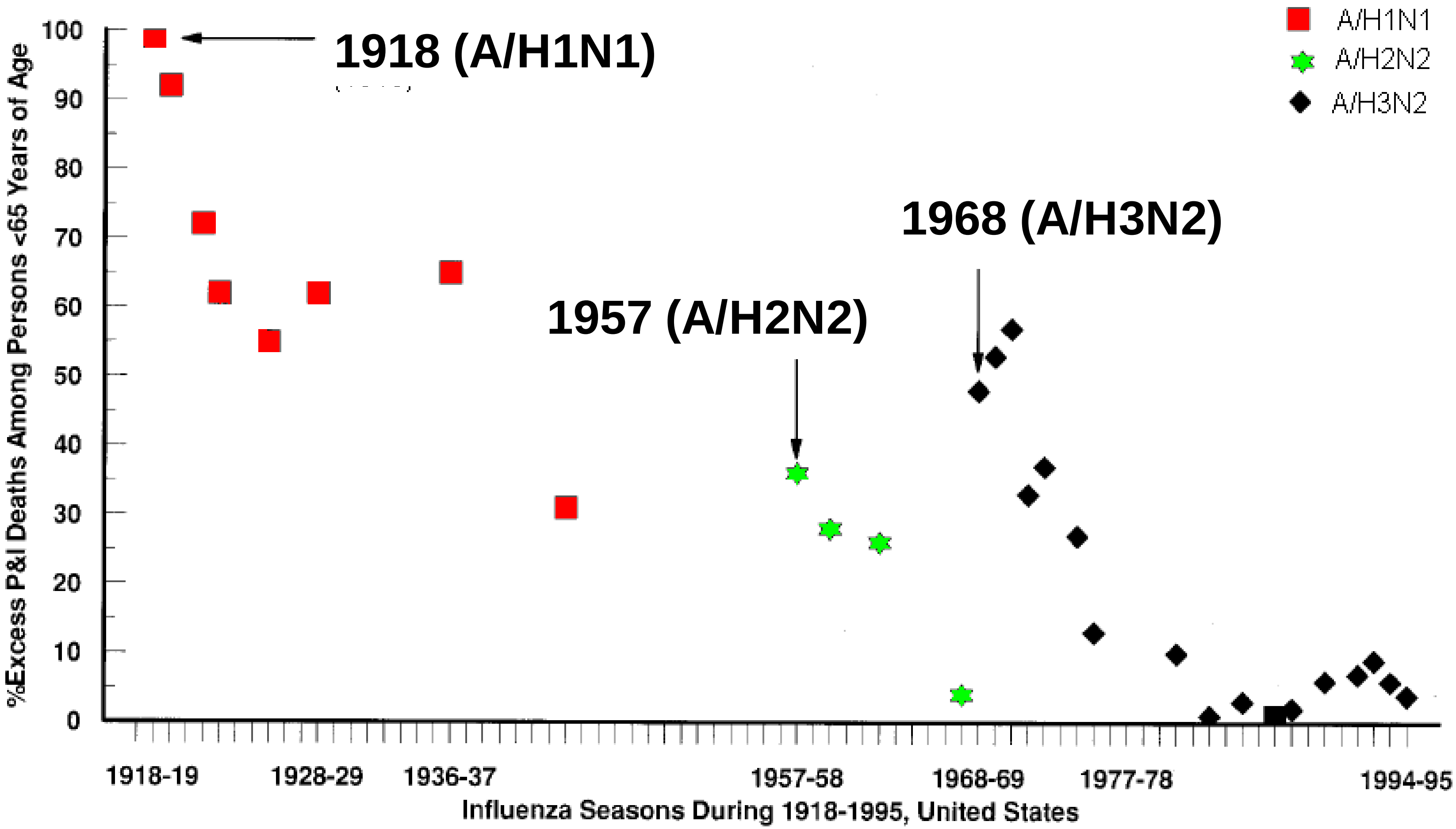
- What are relevant health outcome metrics?
  - Mortality, Years of Life Lost, Labor disruption
- Who is at risk?
  - Epidemics versus Pandemics
- Who benefits directly
  - Differential efficacy of vaccine
- Impact per dose
- Optimization of indirect benefits



Excess seasonal mortality by age group for average of A/H3N2 epidemics

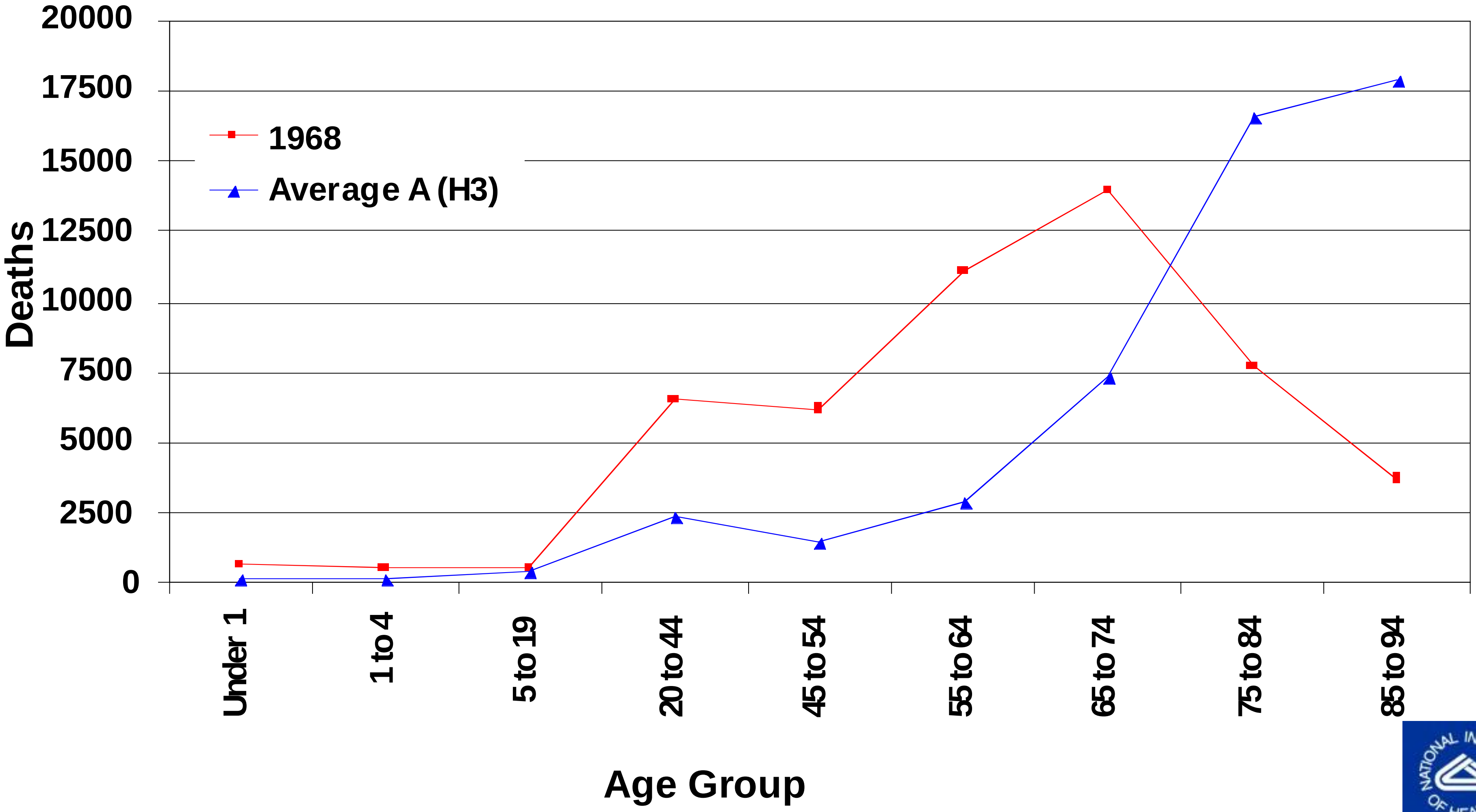


Proportion of mortality in persons < 65 years in Past Influenza Pandemics

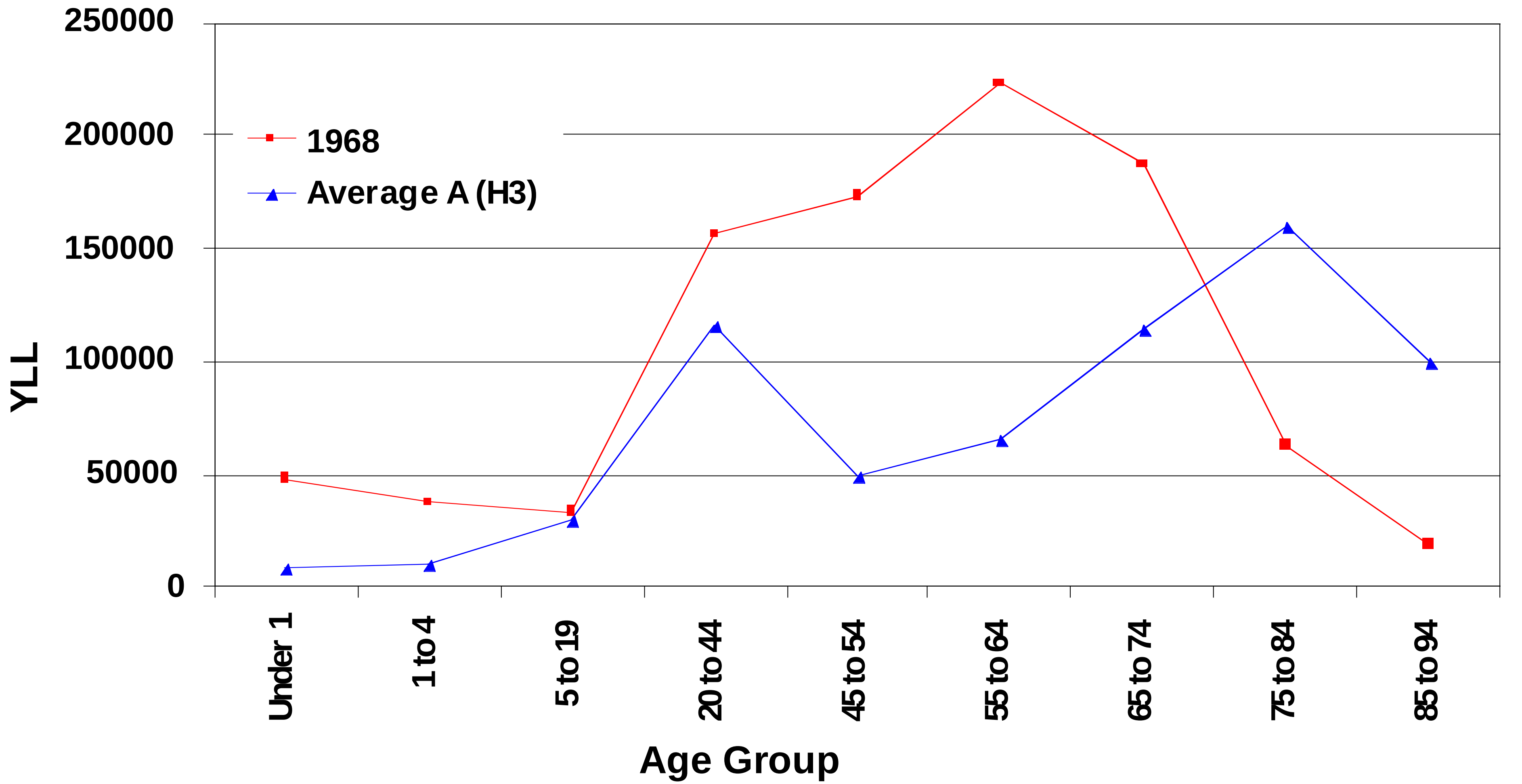


Simonsen L et al, Pandemic versus Epidemic Influenza Mortality: A Pattern of Changing Age Distribution JID, 1998

Excess seasonal mortality by age group for average of A/H3N2 epidemics and 1968 pandemic



Excess seasonal Years of Life Lost by age group for average of A/H3N2 epidemics and 1968 pandemic



Miller MA et al. Prioritization of Influenza Pandemic Vaccination to Minimize Years of Life Lost. JID. 2008.

Pottential Prevented Deaths/YLL of Various Targeted Age Groups in Past Pandemics

Influenza Season	Age Group	Prevented Deaths per 100,000 vaccine doses	Prevented YLL per 10,000 vaccine doses
1918	**Under 45**	394 – 507	2,246 – 2,888
	45-64	**147 - 189**	**694 - 893**
	65+	**26 - 80**	**33 - 102**
1957	**Under 45**	**4.5 – 5.8**	**25 - 32**
	45-64	**32 – 41**	**92 – 118**
	65+	**54 – 167**	**59 - 184**
1968	**Under 45**	**2.9 – 3.8**	**16 – 21**
	45-64	**29 – 37**	**77 – 99**
	65+	**26 – 80**	**28 - 89**
A(H3N2) epidemic	**Under 45**	**1.0 – 1.3**	**5.3 – 6.8**
	45-64	**4.6 – 5.9**	**12 - 15**
	65+	**20 – 62**	**17 - 52**

Miller MA et al. Prioritization of Influenza Pandemic Vaccination to Minimize Years of Life Lost. JID. 2008.

Example 6
Pandemic Response

H1N1 in Mexico

The NEW ENGLAND JOURNAL of MEDICINE

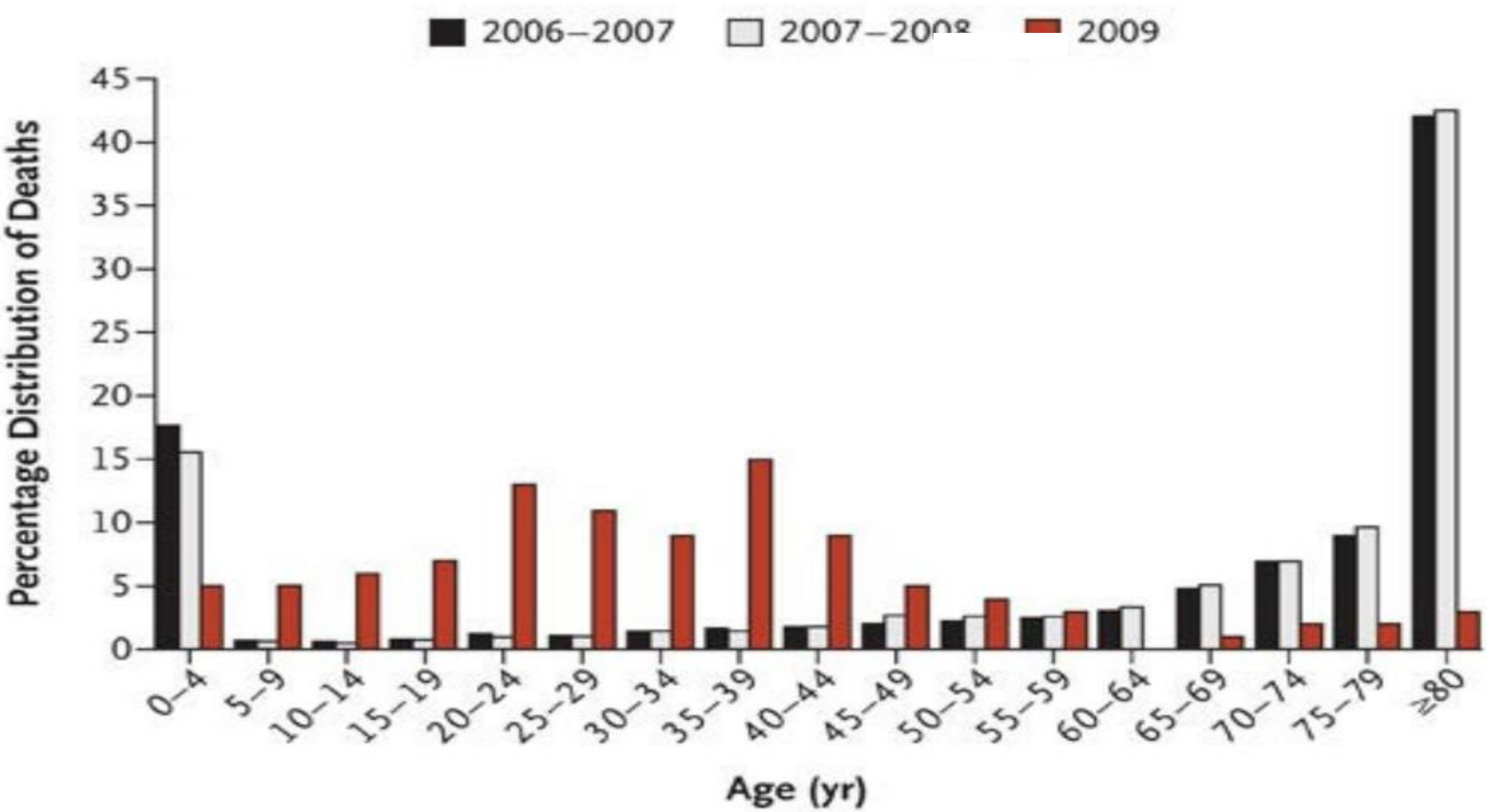
May, 2009

ORIGINAL ARTICLE

Severe Respiratory Disease Concurrent with the Circulation of H1N1 Influenza

Gerardo Chowell, Ph.D., Stefano M. Bertozzi, M.D., Ph.D., M. Arantxa Colchero, Ph.D., Hugo Lopez-Gatell, M.D., Ph.D., Celia Alpuche-Aranda, M.D., Ph.D., Mauricio Hernandez, M.D., Ph.D., and Mark A. Miller, M.D.

N Engl J Med 2009; 361:674-679



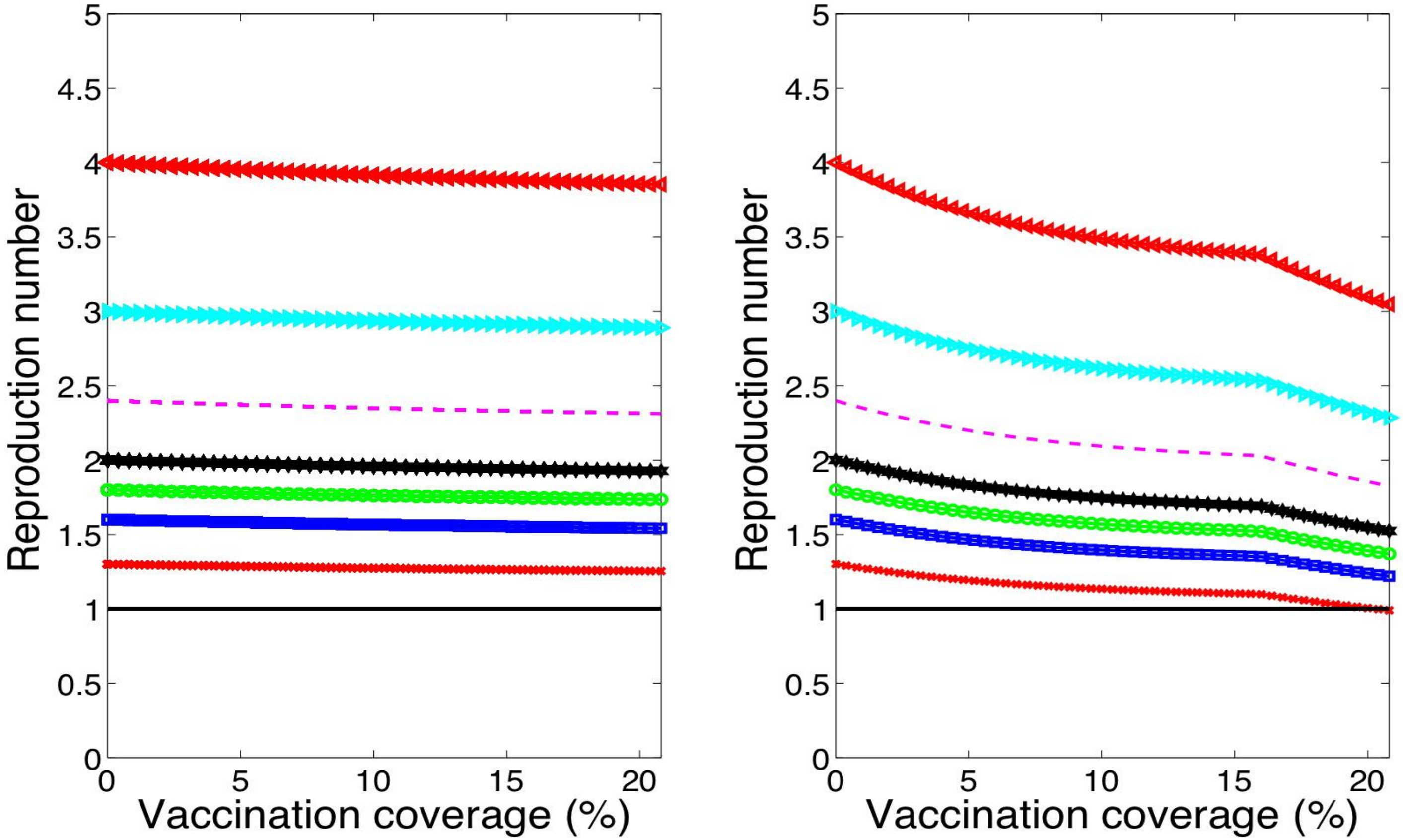
Containment of outbreak?
Mitigate early wave?

- **Would you even want to vaccinate?**
- **Antiviral use**

Who do you vaccinate?

Allocation of resources in real time, costs of each program

Impact of pre-emptive vaccination on transmission rate



0-5 year olds **School age, Young adults, first**

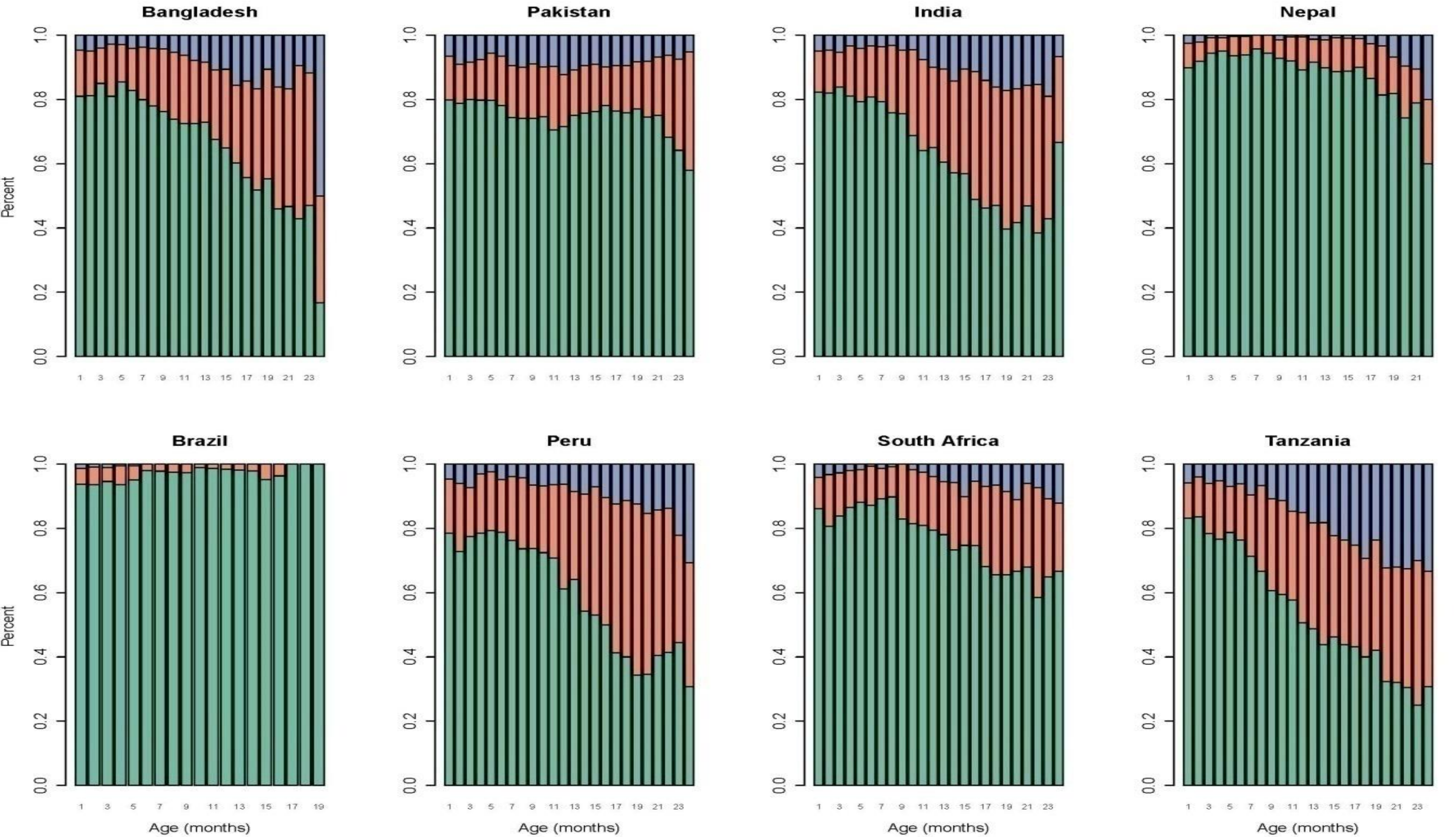
Chowell G et al. Adaptive Vaccination Strategies to Mitigate Pandemic Influenza: Mexico as a Case Study. PLoS one, 2009:

Example 7
Morbidity Outcomes

Vaccines against Growth and Cognition Faltering?

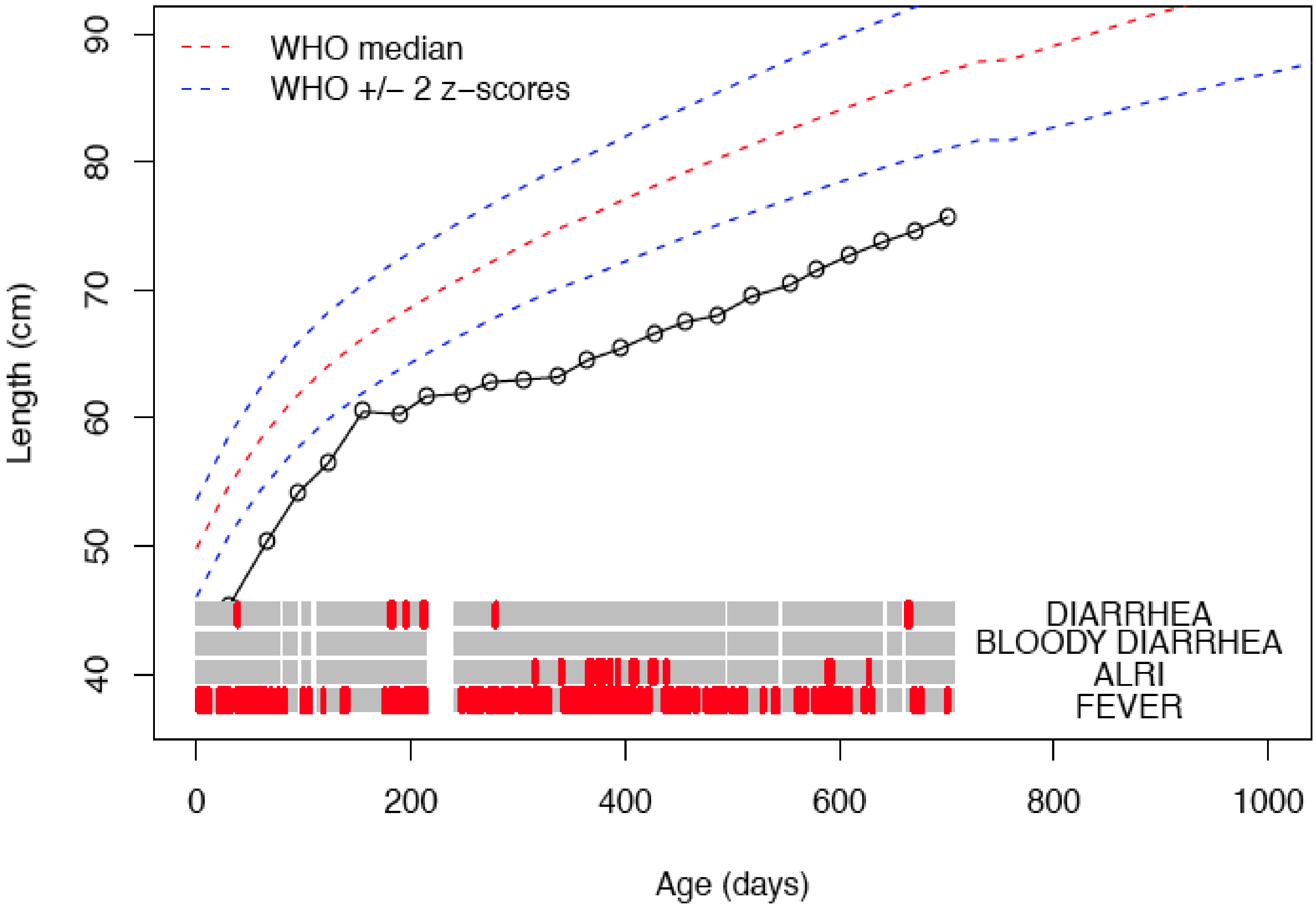
The MAL-ED project

Stunting Prevalence by severity, 0-24 months

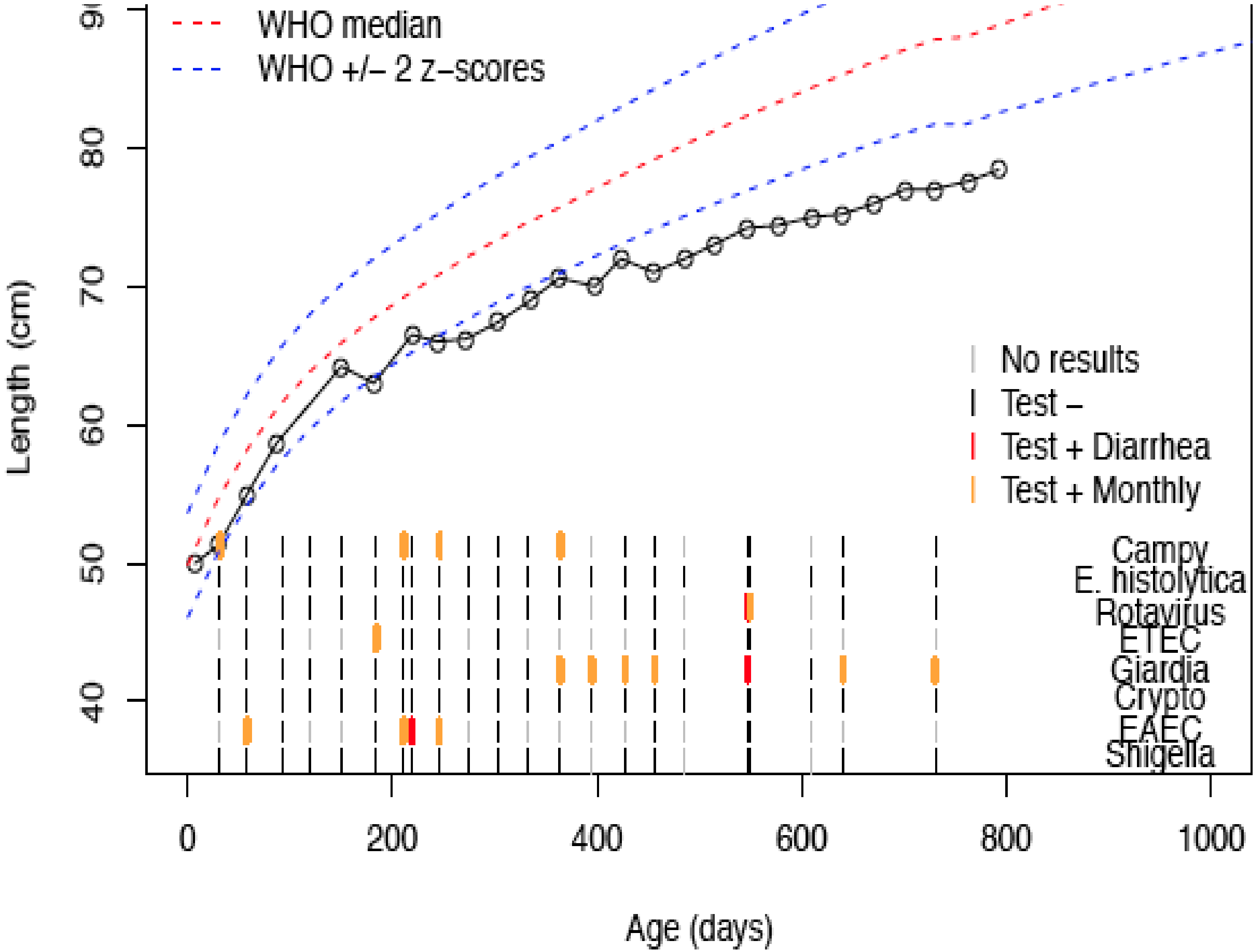


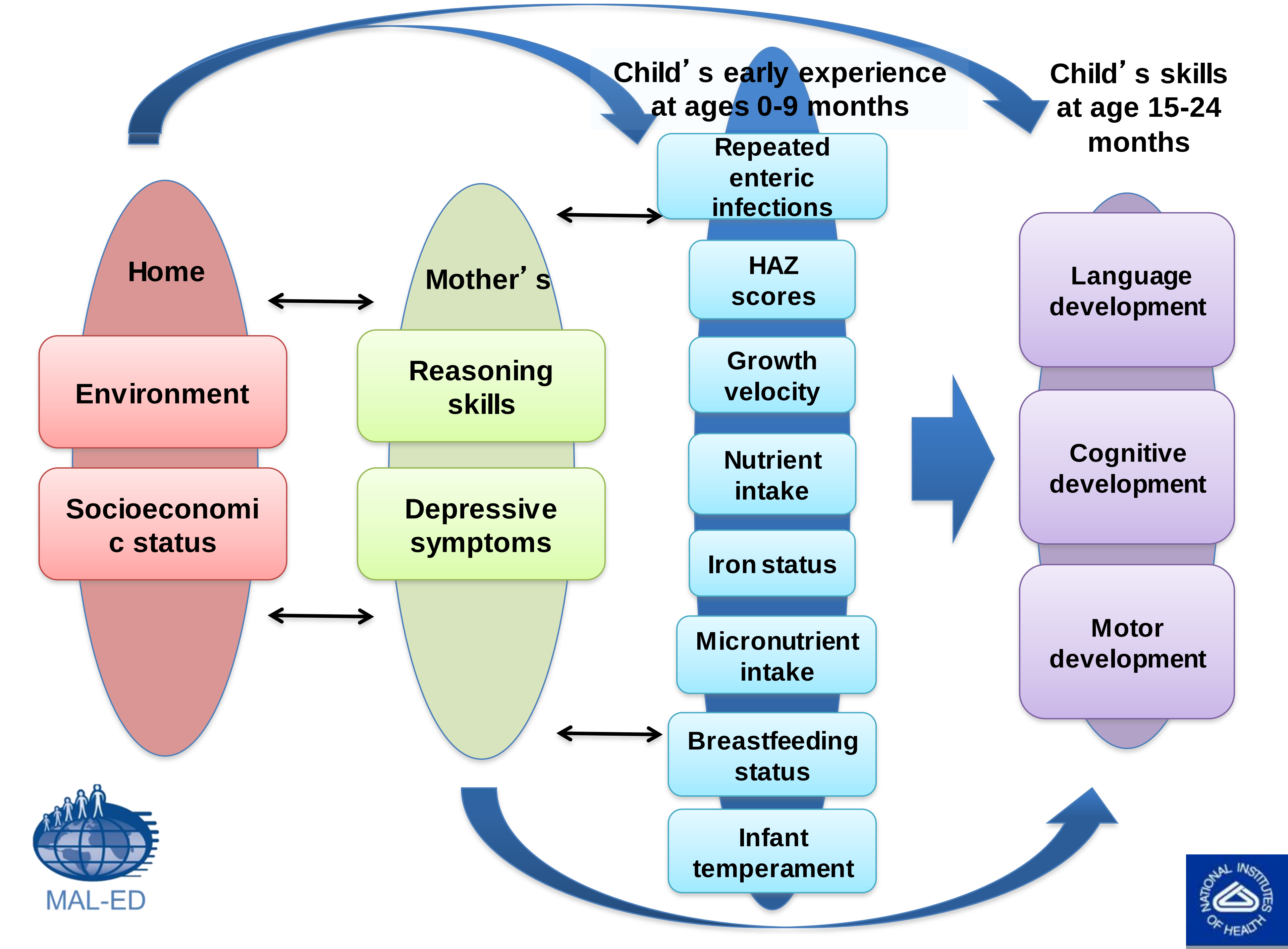
Moderate stunting (orange) and severe (blue)

Length and Growth Curves with Co-morbidities



Length and Growth Curves by Enteric Pathogen





Child’s early experience at ages 0-9 months
Child’s skills at age 15-24 months
Home
Environment
Socioeconomic status
Mother’s
Reasoning skills
Depressive symptoms
Repeated enteric infections
HAZ scores
Growth velocity
Nutrient intake
Iron status
Micronutrient intake
Breastfeeding status
Infant temperament
Language development
Cognitive development
Motor development
MAL-ED

Conclusion

- **Vaccines are Public Health, PH is Politics which require economic analyses to make resource allocation decisions**
  - **Public health marketing and science based decisions to recipients, decision makers in public + private sector**
- **Modeling tools that integrate epidemiology and economics can aid to evaluate value of vaccines (direct and indirect effects), decide amongst strategies, characteristics of ideal vaccines, operational/financial needs, market opportunities**
- **Policy analysis aids in the formulation of directed research to decrease uncertainty**
- **Analyses are best conducted using local epidemiologic and economic assumptions for outcomes relevant to local policy-makers**